

Long-lasting amelioration of visuospatial neglect by prism adaptation

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Summary

It has been shown that unilateral left neglect can be significantly improved for a short time after a short period of adaptation to a prismatic shift of the visual field to the right. In neuropsychological studies, however, there is no evidence demonstrating long-lasting effects following treatment by prism adaptation (PA). The first aim of the present study was to find out whether the short-term amelioration found after prismatic adaptation could be converted into long-term therapeutic improvement. Secondly, we investigated whether the improvement of neglect in standard tests could be generalized to ecological visuospatial tests. Thirdly, the effects of prism adaptation on different spatial domains (far, near and personal space) were evaluated. Fourthly, the influence of PA on high-order visuospatial functions, such as spatial representation, and on a low-order factor, i.e. sensory-motor bias, was investigated. Finally, we investigated the possible correlation between neglect amelioration, the adaptation effect and the visuomotor after-effect, as assessed by a pointing task during and after PA. Seven patients with right hemisphere lesion and left visuospatial neglect were treated with prismatic lenses in twice-daily sessions over a period of 2 weeks. In each training session, patients were required to perform a

pointing task wearing base-left wedge prisms inducing a shift of the visual field to the right by 10°. The presence of visual neglect and the duration of the amelioration achieved were assessed before the treatment and 2 days, 1 week and 5 weeks after treatment by using a standardized battery that included a series of behavioural and ecological visuospatial tests. Six control, untreated patients, matched to the experimental group for gravity and duration of illness, were submitted to the same tests at the same intervals as the experimental patients. The results showed an improvement in the experimental patients' performance after PA, which was maintained during the 5-week period after treatment. The amelioration of neglect was found in standard as well as in behavioural tests and in all spatial domains. In contrast, control patients did not show any improvement in neglect. The amelioration of neglect occurred only in patients who showed the adaptation effect and the after-effect in the pointing task. Neglect amelioration did not occur in one patient who did not show the adaptation effect and had an unstable after-effect. In conclusion, these findings show that prism adaptation is a productive way of achieving long-lasting improvements in neglect treatment.

Keywords: visuospatial neglect; neglect rehabilitation; visuospatial tests; prism adaptation; prism after-effect

Abbreviations: ANOVA = analysis of variance; BIT = Behavioural Inattention Test battery; PA = prism adaptation

Introduction

Unilateral left neglect, a lack of responses to the left side of space, is one of the best single predictors of poor functional recovery following stroke (Kinsella and Ford, 1980; Denes *et al.*, 1982; Gialanella and Mattioli, 1992; Sea *et al.*, 1993). Unilateral neglect is notoriously difficult to rehabilitate. In the last 30 years, various rehabilitation approaches have attempted to improve the recovery of patients with chronic

and persistent unilateral neglect. These approaches can be divided into two classes: rehabilitation procedures based on top-down mechanisms and those based on bottom-up mechanisms.

Rehabilitation procedures based on top-down mechanisms train patients to direct attention to the neglected side (Pizzamiglio *et al.*, 1992; Làdavas *et al.*, 1994; Antonucci

et al., 1995). Pizzamiglio *et al.* (1992) and Antonucci *et al.* (1995) used a variety of visual scanning procedures designed to improve the recovery of patients with chronic and persistent unilateral neglect. They obtained an amelioration of patients' performance in many classical neuropsychological tests as well as in the semistructured scale for the Functional Evaluation of Hemi-Inattention in Extrapersonal Space (Zoccolotti and Judica, 1991; Zoccolotti *et al.*, 1992).

In the study of Lådavas *et al.* (1994), neglect patients were trained to direct attention to the contralesional side of space through the use of central cues that were informative, i.e. they were highly predictive of the location of the imperative stimulus. The treatment brought about an improvement in detecting and pointing out objects located in the left side of space.

These procedures require patients to be aware of their deficit and to have the capacity to voluntarily maintain attention oriented to the affected field, which may be difficult for neglect patients in everyday life.

For this reason, treatments based on bottom-up mechanisms, which do not require the patient to be aware of their difficulty and to have voluntary control of the contralesional space, should be more successful. These rehabilitation procedures use sensory stimulation (vestibular, optokinetic, left-sided transcutaneous mechanical vibration, left-sided electrical nervous stimulation and left-limb proprioceptive stimulation) to enhance the contralesional space. Vestibular stimulation by squirting iced water into the patient's left ear (or warm water into the right ear) has been shown to ameliorate left hemineglect (Rubens, 1985; Cappa *et al.*, 1987; Vallar *et al.*, 1990), as has optokinetic stimulation, in which a leftward-moving background is used to direct the patient's attention automatically to the contralesional side (Pizzamiglio *et al.*, 1990). Transcutaneous mechanical vibration (Karnath *et al.*, 1993) and electrical neural stimulation (Vallar *et al.*, 1995), in which mechanical vibration and electrical stimulation, respectively, are applied to the left neck muscles, also induce partial remission of the visuospatial deficit. Proprioceptive stimulation, using active (Robertson and North, 1993) and passive (Lådavas *et al.*, 1997b; Frassinetti *et al.*, 2001) movements of the contralesional paretic limb, reduces neglect for stimuli presented in contralesional space. However, many of these studies have used only a single application of these sensory manipulations and consequently the amelioration lasted for only a few minutes.

One alternative approach to the rehabilitation of neglect that is based on bottom-up mechanisms is adaptation to a right prismatic shift of the visual field (Rossetti *et al.*, 1998). Rossetti *et al.* (1998) showed that a short period of visuomotor adaptation to a right prismatic shift of the visual field was efficacious in ameliorating visual neglect. In their study, an improvement was observed in traditional neuropsychological tests assessing visual neglect (e.g. cancellation, copying and bisection) and was fully maintained 2 h later. In recent single case studies (e.g. Pisella *et al.*, 2002), the effects

of prism adaptation (PA) have been reported to last up to 4 days. However, no systematic study is available on a group scale demonstrating long-lasting effects following PA treatment.

Therefore, the first aim of the present study was to find out whether the short-term improvement in neglect found by Rossetti *et al.* (1998) could be converted into long-term therapeutic improvement by using their PA procedure. For this reason, a group of neglect patients (experimental patients) was submitted to a treatment which consisted of a procedure similar to that used in the study of Rossetti *et al.* (1998). Patients underwent the treatment in twice-daily sessions over a period of 2 weeks. To assess the efficacy of the training and the duration of its effects, neglect patients performed a battery of visuospatial tests before the treatment and 2 days, 1 week and 5 weeks after the end of the treatment.

The second aim was to investigate whether the results obtained in classical neuropsychological tests can be generalized to ecological tests. Most rehabilitation studies report an amelioration of neglect in standard neuropsychological tests (e.g. cancellation, bisection and drawing) but they ignore ecological tests, which might be more informative about the specific difficulties patients encounter in everyday life. Therefore, in the present study, the effects of PA were evaluated not only in conventional paper-and-pencil tests but also in everyday situations. In particular, we used a battery of tests for spatial deficit [the Behavioural Inattention Test battery (BIT)] (Wilson *et al.*, 1987), which comprises conventional tests (e.g. cancellation, bisection and drawing tests) and behavioural tests (e.g. picture scanning, telephone dialling, menu and article reading, address and sentence copying, telling and setting the time, coin and card sorting and map navigation tests). The difficulties of patients in everyday situations were also assessed by two other ecological tests (room description test and objects reaching test).

The third aim was to evaluate the effects of PA on different spatial domains (far, near and personal space). This was because three types of neglect—far/out-reaching space, near/within-reaching space, and personal or body space—have been found to be dissociable (Rizzolatti and Camarda, 1987; Rizzolatti and Berti, 1990; Halligan and Marshall, 1991; Guariglia and Antonucci, 1992). In the present study, we explored the possibility that PA induces an amelioration of neglect for far and near space but not for personal space. Near and far spaces are better coded retinocentrically and PA might produce a modification of the retinocentric coordinates, because it induces a shift of the visual field. To verify this hypothesis, a different test for each type of neglect was used: the room description test (far space), the Object Reaching test (near space) and the fluff test (personal space).

The fourth aim was to assess whether neglect improvement is due to the amelioration of high-order visuospatial functions rather than a low-order factor, namely the leftward sensory-motor bias of the ipsilesional arm induced by adaptation to the right visual field itself. The initial disorganization of visuomotor behaviour following prismatic exposure is cor-

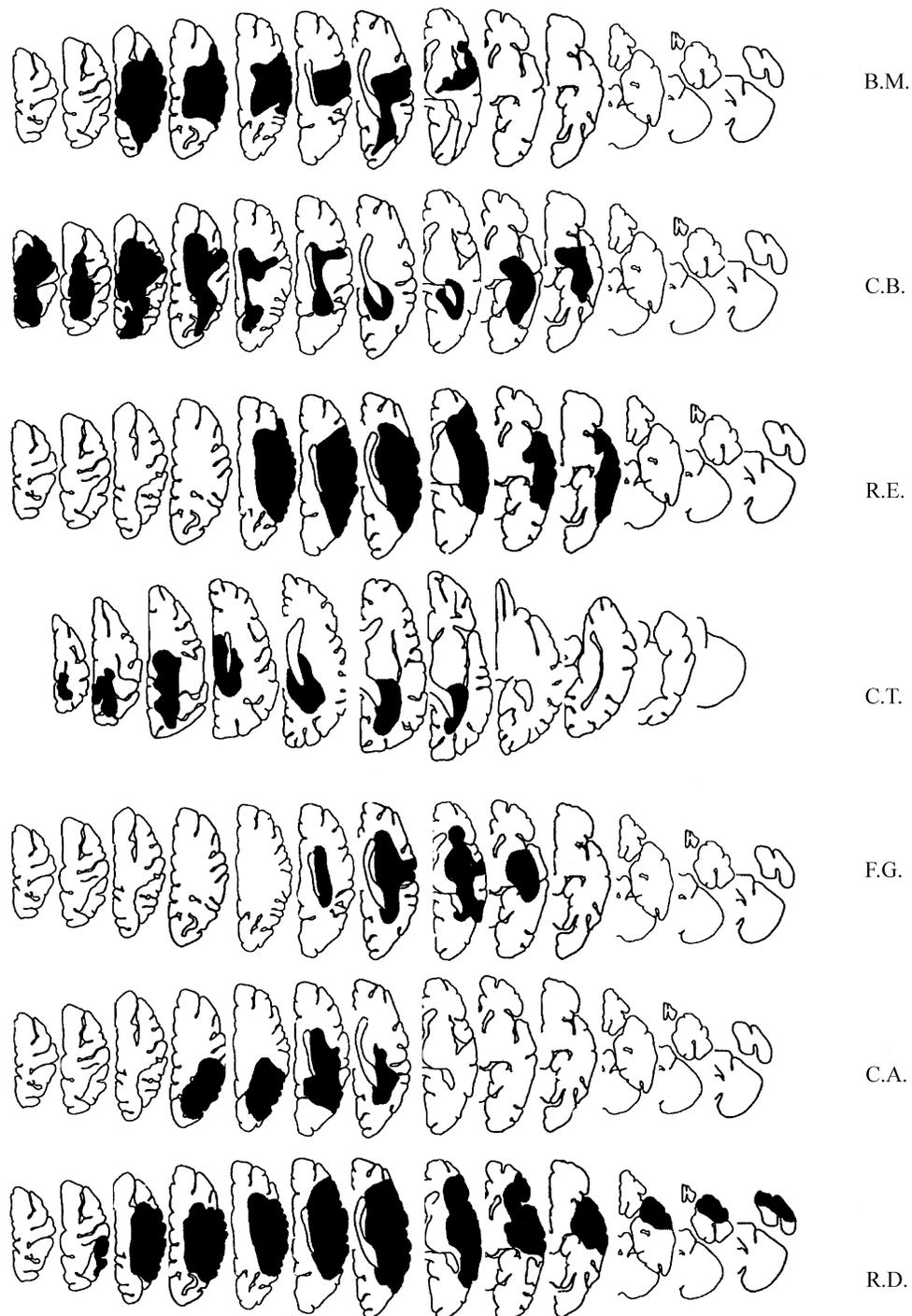


Fig. 1 Brain lesions in experimental patients. The figures show the location of brain damage in each of the experimental patients according to the standard template provided by Damasio and Damasio (1989).

rected during the process of visuomotor adaptation. The major compensatory consequence of this adaptation is a shift of visual and proprioceptive representations, which is reflected in a typical visuomotor bias, the so called after-effect (Held and Gottlieb, 1958): subjects systematically deviate the adapted limb in the direction opposite to the prismatic shift. In the case of adaptation to a right prismatic

deviation, the after-effect consists of a leftward visuomotor bias, which is present in normal subjects as well as in patients with neglect (Rossetti *et al.*, 1993, 1998). If the amelioration of neglect after PA is due to a low-order factor, such as a leftward visuomotor bias, amelioration is expected only in tests performed with the right adapted limb (i.e. cancellation, writing, drawing and objects reaching tests). However, if the

Table 2 Summary of clinical data for experimental and control patients

Group	Case	Age (years), sex	Onset of illness (months)	Left hemianopia	BIT-C (cut-off 129)	BIT-B (cut-off 67)
E	B.M.	71, M	6	–	110	54
E	C.B.	59, F	4	–	72	62
E	R.E.	77, F	3	–	107	24
E	C.T.	41, F	24	+	95	65
E	F.G.	65, M	4	+	66	73
E	C.A.	73, F	5	–	112	32
E	R.D.	70, M	15	–	89	73
C	C.A.	52, M	6	–	119	65
C	R.A.	79, F	4	–	110	71
C	B.A.	58, F	27	–	122	63
C	F.F.	52, M	17	–	99	67
C	S.L.	76, F	3	+	25	6
C	A.A.	59, M	4	+	92	52

E = experimental group; C = control group; BIT-C = BIT conventional; BIT-B = BIT behavioural.

3 months after the cerebral accident) and had no clinical sign of dementia.

Assessment of neglect

All patients underwent a standardized battery of tests for visuospatial deficit (BIT; Wilson *et al.*, 1987), a bell cancellation test (Gauthier *et al.*, 1989), a reading test (Làdavas *et al.*, 1997a) and a modified version of the fluff test (Cocchini *et al.*, 2001) as well as a room description test and an objects reaching test.

BIT

BIT is a battery of tests for spatial deficit and it includes conventional and behavioural tests. The conventional tests are line crossing, letter cancellation, star cancellation, figure and shape copying, line bisection and representational drawing. The behavioural tests, which reflect aspects of daily life activities, are picture scanning, telephone dialling, menu reading, article reading, telling and setting the time, coin sorting, address and sentence copying, map navigation and card sorting. The cut-off scores of the conventional and behavioural tests are 129 (0–146, maximum score 146) and 67 (0–81, maximum score 81), respectively. Patients were classified as having neglect when their score was below the cut-off score.

Bell cancellation test (Gauthier *et al.*, 1989)

Patients were asked to cross out bells printed, along with other objects, on a sheet of A4 paper oriented horizontally. The number of bells omitted was recorded.

Reading test (Làdavas *et al.*, 1997a)

Stimuli were 55 Italian concrete words of at least three syllables and 55 legal non-words obtained by substituting two

letters. For the non-words, the substituted letters were located equally often on the left and on the right side of the stimulus. The length of the stimuli was six letters (10 stimuli), seven letters (16 stimuli), eight letters (34 stimuli), nine letters (22 stimuli), 10 letters (18 stimuli) or 11 letters (10 stimuli). The stimuli, printed in upper-case 18-point Palatino font, were located on the centre of the page (A4 format) and were presented horizontally one at a time. Each letter string was presented twice, once in a list composed of both words and non-words (mixed list) and once in a list composed only of words (words pure list) or of non-words (non-words pure list). The patients were instructed to read the letter strings aloud. Omitting or misreading one or more letter was considered to be an error for the whole letter string.

Fluff test

Patients were blindfolded and seated whilst six pieces of adhesive paper were attached by the experimenter to their clothing on the left part of their body (chest, shoulder, elbow, wrist, knee and hip). Once the blindfold had been removed, patients were asked to remove all the paper pieces attached to their clothes in 2 min. The number of pieces omitted was recorded.

Room description test

A room (3.6 × 2.2 m) was equipped with various items arranged about its midline (seven on the left, seven on the right). The patient sat in his or her wheelchair in the centre of the room with their back to an empty wall. On a table placed in the centre of the room in front of the patient there were four objects, two on the left and two on the right. Along the left and right walls, five similar items were aligned (e.g. a door, a chair, a cupboard, a wastepaper basket and a fire extinguisher). The patient was asked to name the items seen in the room for a period of 2 min. The number of items omitted was recorded.

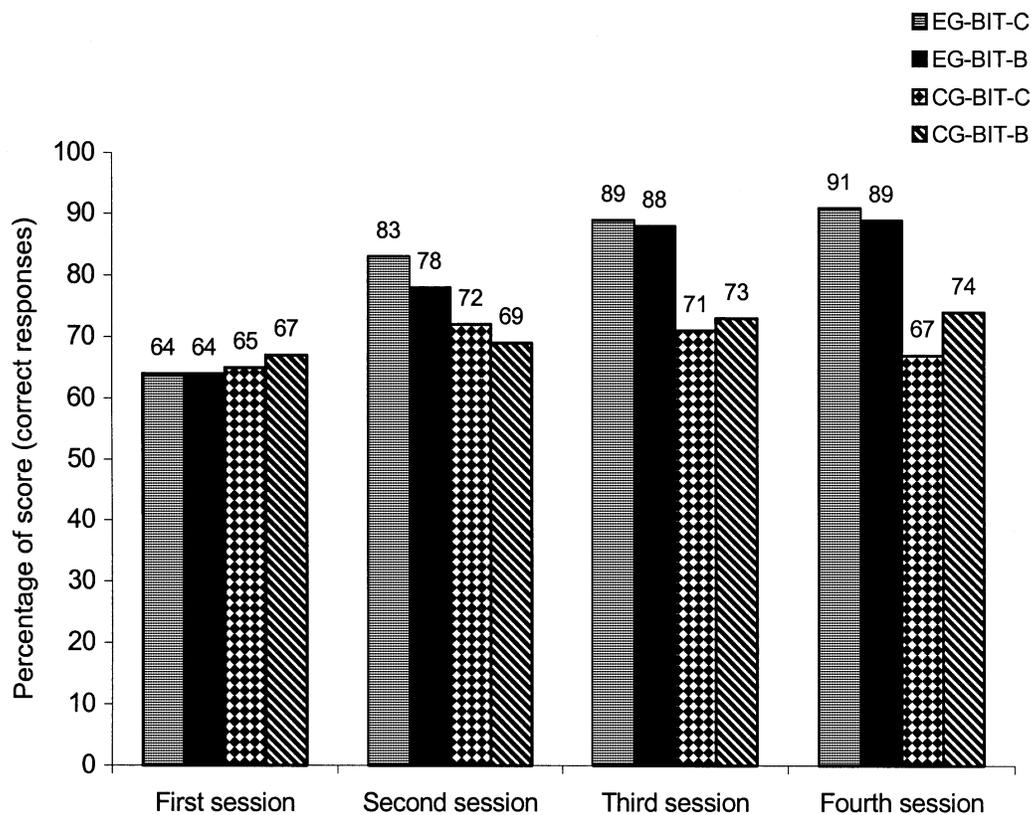


Fig. 2 Effects of prism treatment on the patients' performance (percentage of correct responses) in the BIT battery (BIT-C = BIT conventional; BIT-B = BIT behavioural) for the experimental group (EG) and the control group (CG) as a function of time: before treatment (first session) and 2 days, 1 week and 5 weeks after treatment (second, third and fourth sessions, respectively).

Objects reaching test

Twenty-four common objects (soap, razor, pen, lamp, fork, etc.) were laid out on a table (85 × 85 cm) in front of the patient with its midpoint in line with that of the patient. The objects were arranged in four rows and six columns (three on the left and three on the right). The patient had to touch and name all the objects on the table for a period of 2 min. The number of objects omitted was recorded.

The assessment of neglect was verified in four different sessions. The first baseline session was to verify the presence and amount of neglect and was performed before the treatment began. The remaining sessions were used to verify the effect of PA on neglect; they were conducted 2 days (second session), 1 week (third session) and 5 weeks (fourth session) after the end of treatment. Experimental and control groups were tested by following the same testing procedure and the same time interval. Therefore, control patients were also tested in four sessions: baseline (first session) and 2 weeks (second session), 3 weeks (third session) and 7 weeks (fourth session) after the baseline session.

Motricity Index (Demeurisse et al., 1980)

To evaluate the effectiveness of the prism treatment on the patients' motor recovery, a standardized mobility measure

was adopted—the Motricity Index. Because it was introduced late in our experimental procedure, only two of the experimental patients (F.G. and C.A.), but all control patients, were evaluated with the Motricity Index. It was administered before and after the treatment, at the same time intervals as those used in the neglect testing sessions.

The Motricity Index is a measure of motor impairment of the trunk and the right and left hemisoma (upper and lower limb). Each component part of the index, scored 0–100, expresses the strength of the part of the body that is evaluated.

Rehabilitation procedure

Patients were seated at a table. In front of them on the table there was a wooden box (height 30 cm, depth 34 cm at the centre and 18 cm at the periphery, width 72 cm). The box was open on the side facing the patient and on the opposite side, facing the experimenter. A visual target (a pen) was presented manually by the experimenter at the distal edge of the top face of the box. The visual target was presented randomly in one of three possible positions: a central position, straight ahead in front of the patient (0°), and in a lateral position to the left or right of the patient's body midline (–21° and +21°, respect-

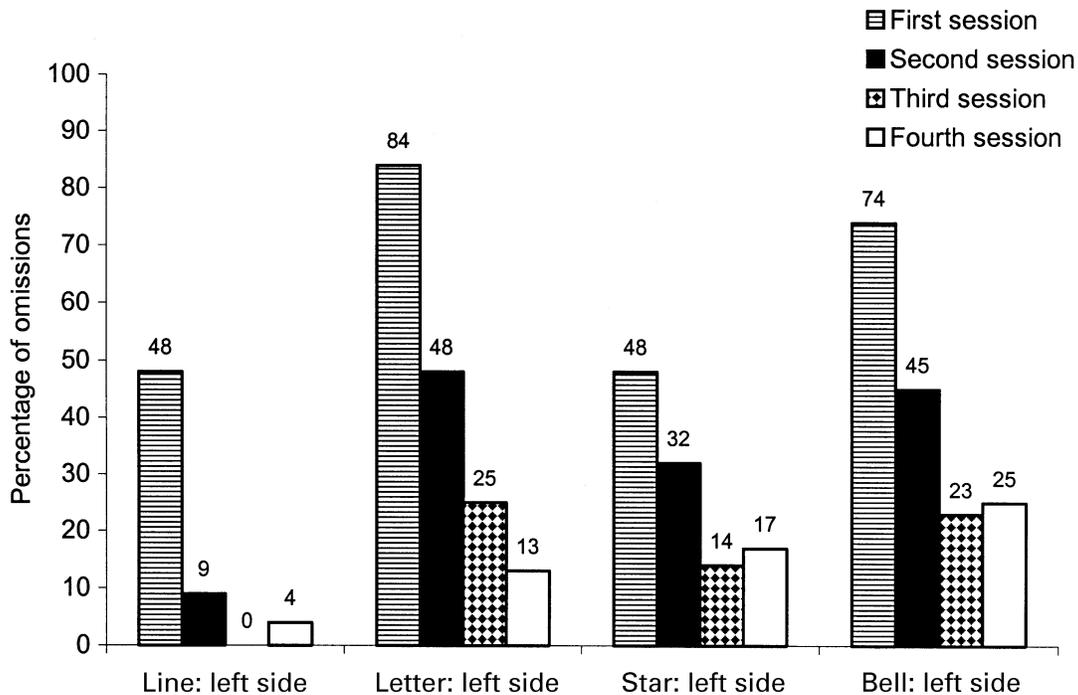


Fig. 3 Effects of prism treatment on patients' performance in cancellation tests. Percentage of omissions on the left side for the experimental group in the line, letter, star and bell cancellation tests as a function of time: before treatment (first session) and 2 days, 1 week and 5 weeks after treatment (second, third and fourth sessions, respectively).

ively). The external edge of the top face of the box was graduated (in centimetres) and the experimenter could therefore ascertain and quantify the patients' spatial accuracy in pointing.

Patients were asked to keep their right, ipsilesional hand on their chest, at the level of the sternum (hand starting position) and to point with the index finger of the same hand towards the pen, at a fast but comfortable speed. The movement of the patient's pointing arm was executed below the top face of the wooden box, so that they could not see the arm's trajectory. Once the experimenter had recorded the patient's pointing performance, the patient retrieved the arm and prepared for the succeeding trial.

Patients underwent treatment in two daily sessions (10 sessions a week), which took about 20 min each, over a period of 2 weeks, giving a total of 20 sessions.

The pointing task was performed in three experimental conditions: Pre-exposure, Exposure and Post-exposure.

Pre-exposure condition

In this condition, patients were required to point with their index finger towards 60 targets presented randomly in one of three possible positions (20 targets at the centre, 20 at the right and 20 at the left). Patients performed half of the trials with visible pointing (see Exposure condition) and half of the trials with invisible pointing (see Post-exposure condition).

Exposure condition

Patients performed the task wearing prismatic goggles. The goggles were fitted with wide-field, prismatic lenses, inducing a 10° shift of the visual field to the right. Patients were asked to point rapidly with their right index finger to 90 targets presented in random order in each of three possible positions (30 targets at the centre, 30 on the right and 30 on the left). The pointing movement was hidden below the top face of the box, apart from the final part of the movement where the index finger emerged beyond the distal edge of the top face of the box (visible pointing).

Post-exposure condition

Immediately after the removal of the prism, the patients were required to point to 30 targets (10 targets at the centre, 10 on the right and 10 on the left). The pointing movement was performed below the top face of the box so that the index finger was not visible at any stage (invisible pointing).

All conditions were run in each of the two daily sessions, with the exception of the visible pointing Pre-exposure condition, which was performed only in the first session of each week.

Statistical analysis

To verify the presence and the duration of amelioration of neglect after PA, statistical analysis was performed on the

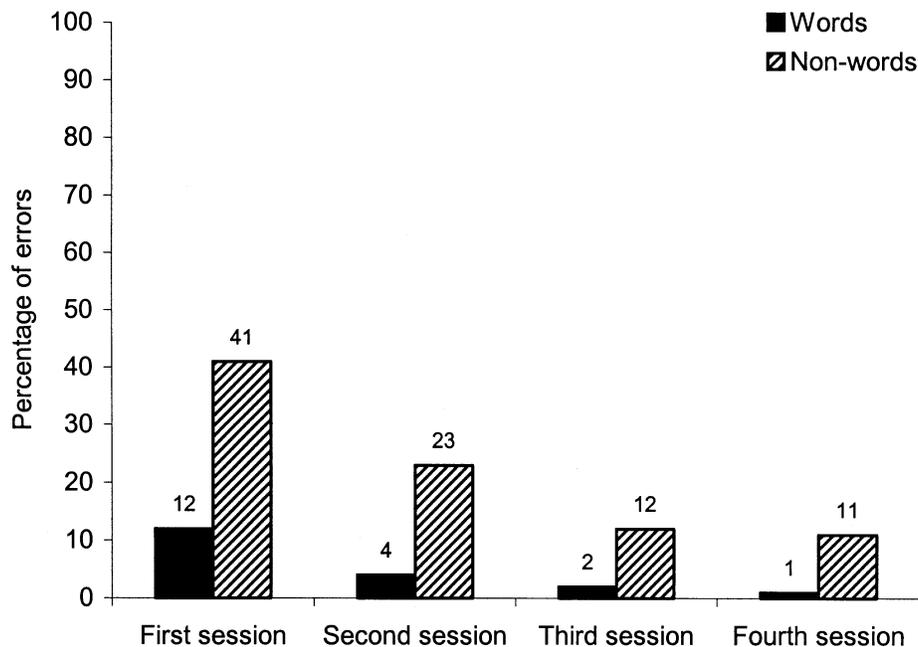


Fig. 4 Effects of prism treatment on patients' performance in the reading test. Percentage of errors for the experimental group in word and non-word reading as a function of time: before treatment (first session) and 2 days, 1 week and 5 weeks after treatment (second, third and fourth sessions, respectively).

results obtained by the two groups of patients (experimental and control groups) in each of the five tests that assessed visual neglect. For the experimental group, only patients who showed the adaptation effect were analysed as a group. Patient R.D., who did not show the adaptation effect, was analysed separately. In addition to analysis of variance (ANOVA), pairwise comparisons were conducted with the Newman-Keuls test when necessary. The level of significance was always set at 0.05.

Results

BIT

To verify the effect of treatment on performance in the conventional and behavioural tests, a two-way ANOVA was carried out on the BIT score (percentage of correct responses), converted into arcsin values, for each of the two groups of patients. It is worth mentioning that this score is based on correct responses. Test (conventional and behavioural) and session (first, second, third and fourth) were the main factors.

Experimental group

Session was the sole significant factor [$F(3,15) = 34$; $P < 0.000001$]. *Post hoc* comparisons revealed an amelioration of neglect when the results for the first session (64%) were compared with those for the second (80%, $P < 0.0003$), third (88%, $P < 0.0002$) and fourth (90%, $P < 0.0002$) sessions. Moreover, the improvement obtained in the third and fourth

sessions (1 and 5 weeks after treatment, respectively) was greater than that found in the second session (2 days after treatment) ($P < 0.01$ and $P < 0.003$, respectively) (Fig. 2). All patients showed the effect.

Control group

Session was not significant. The patients' performance in the first session (66%) did not differ from that in the second (70%), third (72%) and fourth (70%) sessions (Fig. 2).

Cancellation tests

To assess the effect of treatment on cancellation tests, an ANOVA was performed for each of the two groups of patients (experimental and control groups) on the results obtained in the line, letter, star and bell cancellation tests (the first three are subtests of the conventional component of the BIT series). The dependent variable was the number of incorrect responses, i.e. omission errors. The analysis was performed on the percentages of target stimuli omitted, converted to arcsin values. The main effects were side (left and right), test (line, letter, star and bell cancellation) and session (first, second, third and fourth).

Experimental group

The ANOVA revealed a significant effect of side [$F(1,5) = 153.4$; $P < 0.00004$]: omissions on the left were more numerous (32%) than omissions on the right (5%). Test [$F(3,15) = 6.25$; $P < 0.006$] was also significant. *Post hoc*

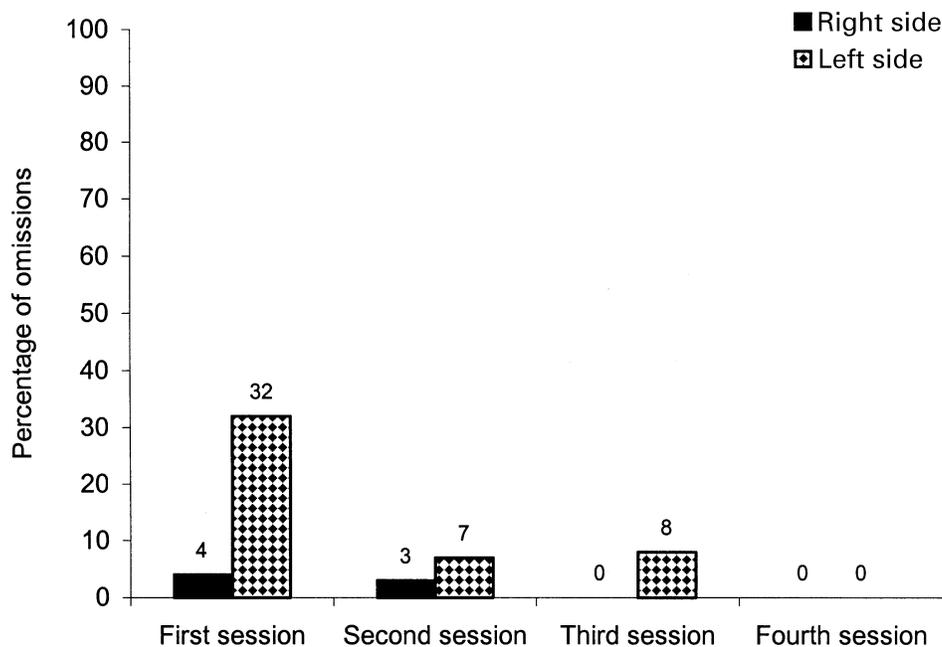


Fig. 5 Effects of prism treatment on patients' performance in the ecological tests. Percentage of omissions on the left and right sides for the experimental group in the room description and objects reaching tests as a function of time: before treatment (first session) and 2 days, 1 week and 5 weeks after treatment (second, third and fourth sessions, respectively).

comparisons revealed a minor number of omissions in the line crossing test (8%) compared with the letter (25%, $P < 0.008$), star (16%, $P < 0.04$) and bell (24%, $P < 0.007$) cancellation tests. The last three tests did not differ significantly. Session (first, second, third and fourth) [$F(3,15) = 19.66$; $P < 0.00001$] was significant. *Post hoc* comparisons showed a reduction in omissions in the second (18%, $P < 0.0007$), third (9%, $P < 0.0002$) and fourth (8%, $P < 0.0002$) sessions compared with the first session (38%). More importantly, the interaction of session with side was significant [$F(3,15) = 9.8$; $P < 0.0007$]. Left side omissions in the first session (63%) were more numerous than omissions in the second (33%, $P < 0.0002$), third (16%, $P < 0.0002$) and fourth (15%, $P < 0.0002$) sessions. No difference was found between omissions on the right side before treatment (first session, 12%) and after treatment (second session, 3%; third session, 3%; fourth session, 2%) (Fig. 3). All patients showed the effect.

Control group

The ANOVA revealed a significant effect of side [$F(1,5) = 7.5$; $P < 0.04$]: omissions on the left were more numerous (41%) than omissions on the right (19%). Test [$F(3,15) = 23.69$; $P < 0.000006$] was also significant. *Post hoc* comparisons revealed a minor number of omissions in line crossing test (10%) compared with the letter (37%), star (30%) and bell (44%, $P < 0.0002$ for all comparisons) cancellation tests. The last three tests did not differ significantly. Session was not significant: omissions in the first session (35%) did not differ from omissions in the second (26%), third (31%) and fourth (30%) sessions.

Reading test

To verify the effect of PA on neglect dyslexia, ANOVA was performed for each group of patients on the percentages of reading errors, with the following main effects: list (pure and mixed), type of stimulus (words and non-words) and session (first, second, third and fourth).

Experimental group

Type of stimulus was significant [$F(1,5) = 9.08$; $P < 0.03$]: patients made more errors with non-words (22%) than with words (5%). Session was also significant [$F(3,15) = 6.22$; $P < 0.006$]. A reduction in errors was found after treatment in the second (13%, $P < 0.03$), third (7%, $P < 0.007$) and fourth (6%, $P < 0.008$) sessions compared with the first session (27%). The interaction of type of stimulus with session was significant [$F(3,15) = 3.68$; $P < 0.04$]. *Post hoc* comparisons showed that non-word reading was significantly worse in the first session (41%) than in the second (23%, $P < 0.002$), third (12%, $P < 0.0003$) and fourth (11%, $P < 0.0003$) sessions. Corresponding values for reading words did not differ significantly between the first (12%), second (4%), third (2%) and fourth (1%) sessions (Fig. 4).

Control group

Type of stimulus was significant [$F(1,5) = 15.6$; $P < 0.01$]: patients made more errors with non-words (15%) than with words (1%). Session was not significant: patients made more or less the same number of reading

errors in the first (9%), second (11%), third (9%) and fourth (5%) sessions.

Fluff test

Two one-way ANOVAs (one for the experimental group and one for the control group) were carried out with session (first, second, third and fourth session) as the main factor. The dependent variable was the number of errors, i.e. omitted targets.

Experimental group

Session did not reach significance [$F(3,15) = 2.55$; $P < 0.09$], although there was a trend for omissions to be more numerous before treatment (14%) than after treatment, i.e. in the second (5%), third (0%) and fourth (0%) sessions. However, it is worth noting that only four of the six patients showed personal neglect before treatment and all of them showed an improvement after treatment.

Control group

Session was not significant: the number of omissions in the first session (11%) did not differ from the number in the second (19%), third (19%) and fourth (11%) sessions. Only two of the five patients (R.A. and S.L.) showed personal neglect and they both showed a worsening of their performance in the second and third sessions.

Room description and objects reaching tests

To verify the effect of treatment on these tests, one ANOVA for each group of patients (experimental and control group) was performed on the percentages of omitted targets, converted to arcsin values, with test (room description and objects reaching), side (left and right) and session (first, second, third and fourth) as main effects.

Experimental group

Session was the sole significant factor [$F(3,12) = 10.10$; $P < 0.001$]. *Post hoc* comparison revealed a reduction of omissions in the second (5%, $P < 0.007$), third (4%, $P < 0.007$) and fourth (0%, $P < 0.001$) sessions compared with the first session (18%). No difference was found among the second, third and fourth sessions. The interaction of side with session was also significant [$F(3,12) = 4.8$; $P < 0.002$]. Left-side omissions were more numerous in the first session (32%) than in the second (7%, $P < 0.002$), third (8%, $P < 0.001$) and fourth (0%, $P < 0.0005$) sessions. No difference was found between omissions on the right side before treatment (first session, 4%) and after treatment (second session, 3%; third session, 0%; fourth session, 0%) (Fig. 5).

Control group

Session was not significant: the number of omissions in the first session (10%) did not differ from the numbers in the second (14%), third (11%) and fourth (8%) sessions.

Motricity Index

One ANOVA with group (experimental and control) as the between-subjects factor and body part (left hemisoma and trunk) and session (first, second, third and fourth) as within-subjects factors was carried out on the Motricity Score (maximum score 100 for each body part). Body part was significant [$F(1,6) = 37.72$; $P < 0.0009$]: motor impairment was more severe for left hemisoma (score 37) than for the trunk (score 77). No difference was found between the experimental and control groups (55 versus 59). The interaction of group with body part was significant [$F(1,6) = 13.02$; $P < 0.01$]. The left hemisoma was more impaired in the experimental than in the control group (23 versus 51, $P < 0.03$), whereas the trunk was equally impaired in the two groups (88 versus 67). Moreover, in the experimental group motor deficit was more severe for the left hemisoma than for the trunk ($P < 0.002$); no significant difference was found in the control group between the left hemisoma and the trunk. The main effect and interactions involving session were not significant.

To demonstrate the functional relationship between neglect amelioration and PA, the adaptation effect and the visuomotor after-effect in the pointing task were also analysed. Three ANOVAs were performed to assess the presence of the adaptation effect during prism exposure, the presence of the after-effect following prism exposure and the duration of the after-effect. The adaptation effect is the tendency to compensate, during prism exposure, for prism-induced error; the after-effect is the tendency to point to the direction opposite the optical displacement induced by prisms, when prisms are removed. Pointing displacement is indicated by ‘-’ when directed to the left and by ‘+’ when directed to the right with respect to the object’s actual location. Whenever necessary, pairwise comparisons were conducted using the Newman-Keuls test.

Adaptation effect

To verify whether patients were actually adapted to the rightward deviation induced by prism exposure, we compared their displacement in the Pre-exposure condition with that in the Exposure condition. If patients in the Exposure condition compensate for the rightward displacement induced by prism exposure (adaptation), no difference should be found between the Pre-exposure and Exposure conditions. The dependent measure under consideration in this analysis was the mean displacement (expressed as a visual angle) of visible pointing before treatment (Pre-exposure condition) and in the first

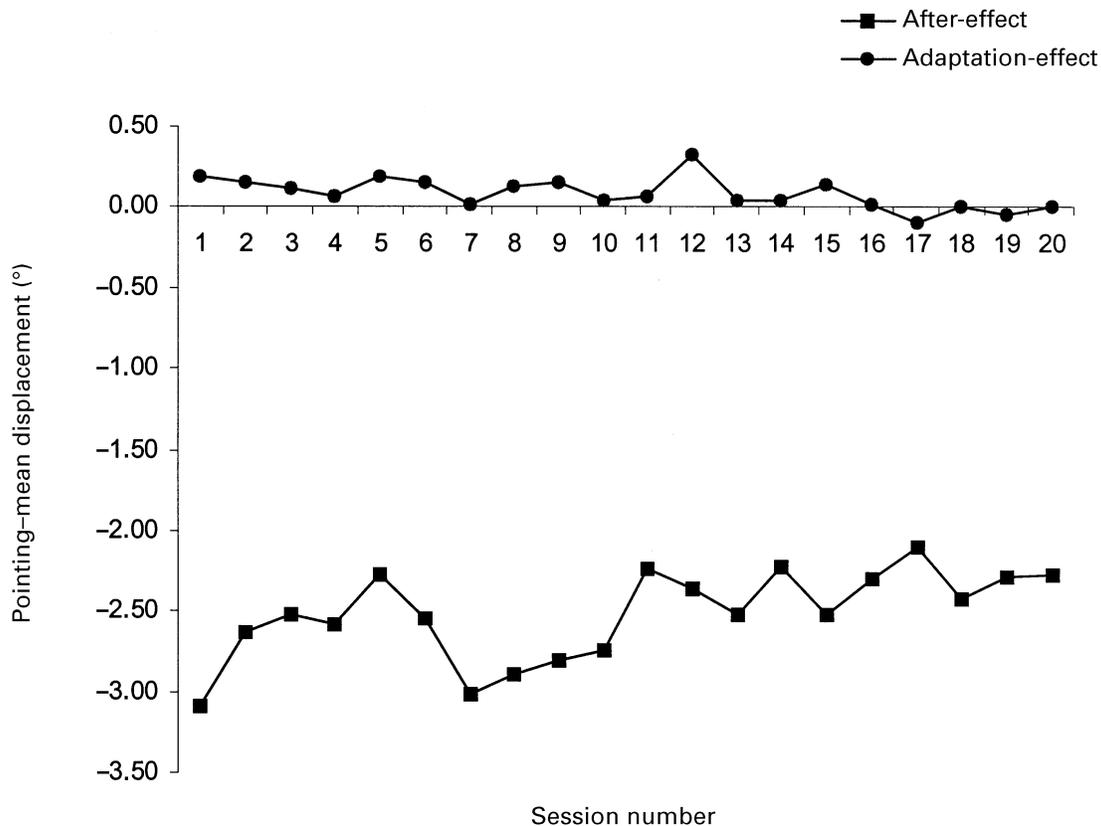


Fig. 6 Adaptation effect and the after-effect over 2 weeks of prism treatment. Mean displacement (expressed as a visual angle) of the patients' pointing responses in the Exposure condition (i.e. the adaptation effect) and the After-exposure condition (i.e. the after-effect) plotted against session number.

session of the first and second weeks of treatment (Exposure condition—first week and Exposure condition—second week). A 3×3 ANOVA was performed with the following main effects: condition (Pre-exposure condition, Exposure condition—first week and Exposure condition—second week) and target position (left, centre and right). Condition was not significant, indicating that pointing deviation did not differ among the Pre-exposure condition (0.3°), the Exposure condition—first week (0.2°) and the Exposure condition—second week (0.2°). Target position was not significant.

In order to verify the consistency of the adaptation effect during prism exposure, an analysis was conducted on the mean displacement (expressed as a visual angle) of the patients' visible pointing in the first three and the last three trials of the Exposure conditions. ANOVA was carried out with the following main effects: condition (Pre-exposure condition, Exposure condition—first week and Exposure condition—second week), target position (left, centre and right) and trials (first and last). The main effect of trials was significant [$F(1,5) = 34.1$; $P < 0.002$]: the adaptation effect was more evident in the last (0°) than in the first (1.5°) three trials. Moreover, the interaction of trials with condition was significant [$F(2,10) = 25.6$; $P < 0.0001$]. The difference between the first three and the last three trials was greater in the first (2.5° versus 0° , $P < 0.0002$) than in the second (1.7°

versus 0° , $P < 0.0007$) week of treatment. The same comparison was not significant in the Pre-exposure condition (0.2 versus 0.3).

After-effect

To verify the presence and amount of after-effect, we compared the patients' displacement in the Pre-exposure and Post-exposure conditions. The dependent measure in this analysis was the mean displacement (expressed as a visual angle) of the patients' invisible pointing responses before treatment (Pre-exposure condition) and in each session of the first and second weeks of treatment (Post-exposure condition—first week and Post-exposure condition—second week). A 3×3 ANOVA was performed with the following main effects: condition (Pre-exposure condition, Post-exposure condition—first week and Post-exposure condition—second week) and target position (left, centre and right). Condition was significant [$F(2,10) = 29.4$; $P < 0.00007$]. *Post hoc* comparisons showed the presence of a significant leftward after-effect in the Post-exposure condition in both the first and the second week of treatment (-2.8° and -2.6° , respectively) compared with the Pre-exposure condition (0° ; $P < 0.0003$ and $P < 0.0002$, respectively).

In order to verify the consistency of the after-effect in the Post-exposure conditions, an analysis was conducted on the mean displacement (expressed as a visual angle) of the invisible pointing response in the first three and last three trials of the Post-exposure condition. ANOVA was carried out with the following main effects: condition (Pre-exposure condition, Post-exposure condition—first week and Post-exposure condition—second week), Target position (left, centre and right) and trials (first and last). The main effect of trials and the interactions involving trials were not significant; indeed, the after-effect did not differ in the first three (-1.7°) and in the last three (-1.8°) trials.

The time course of both the adaptation effect and the after-effect with respect to different sessions is shown in Fig. 6.

Duration of the after-effect

To verify the duration of the post-adaptation after-effect, an ANOVA was performed on the patients' mean displacement expressed as a visual angle with interval as the main effect. The patients' displacement (invisible pointing) was measured before the beginning of training (baseline condition), immediately after treatment and 6, 12, 84, 168 and 720 h after treatment. Six hours is the interval between the morning and afternoon sessions of the same day; 12 h is the interval between an afternoon session and the morning session of the following day; 84 h is the interval between the last afternoon session of the first week and the first morning session of the second week; 168 h is the interval between the last training session of the second week and the test session after a rest of 1 week; and 720 h is the interval between the last training session and the test session after a rest period of 1 month. Interval was significant [$F(6,30) = 9.34$; $P < 0.000008$]. *Post hoc* comparisons showed a leftward deviation of pointing immediately after treatment (-2.7° , $P < 0.0001$) and 6 h (-1.4° , $P < 0.03$) and 12 h (-1.3° , $P < 0.03$) after treatment compared with the baseline condition (0°). No difference was found between the baseline condition (0°) and 84, 168 and 720 h after treatment (-1° , -1° and 0° , respectively). The leftward deviation found immediately after treatment (-2.7°) was significantly greater than that found 6 h (-1.4° , $P < 0.005$), 12 h (-1.3° , $P < 0.009$), 84 h (-1° , $P < 0.004$), 168 h (-1° , $P < 0.002$) and 720 h (0° , $P < 0.0001$) after treatment.

Patient R.D.

A different pattern of results was observed in Patient R.D., who did not show an adaptation effect. His performance was evaluated only before treatment (first session) and 2 days after treatment (second session). He was not tested 1 and 5 weeks after treatment because no improvement was found immediately after PA treatment.

R.D.'s results in the visuospatial tests

BIT

Fisher's exact test was conducted separately on the conventional and behavioural BIT scores to compare patients' performance before treatment (first session) and after treatment (second session). In the BIT conventional tests, performance in the second session (71% of correct responses) was better than in the first session (61%; $P < 0.04$). In the BIT behavioural tests, performance in the second session (68%) was worse than in the first session (90%; $P < 0.0001$). Thus, R.D. showed mild improvement in his performance after treatment in the conventional tests and worsening of his performance in the behavioural tests.

Cancellation tests

Fisher's exact test was performed on omission errors in each cancellation test (line, letter star and bell cancellation tests). No difference between the first and second sessions was found for the line cancellation test (22 versus 17%), letter cancellation test (23 versus 10%) and star cancellation test (52 versus 44%). However, in the bell cancellation test there were fewer omissions in the second session (31%) than in the first session (54%; $P < 0.03$).

Reading test

R.D. did not make reading errors with words. Consequently, statistical analysis was conducted only on non-word reading errors. Fisher's exact test was performed separately for the pure and mixed lists with respect to non-word reading errors. In the pure list, R.D. made more non-word reading errors in the first (36%) than in the second session (11%; $P < 0.002$). In the mixed list, no difference was found in non-word reading errors between the first (18%) and second (11%) sessions.

Pointing task

Adaptation effect

The dependent measure in this analysis was the difference (expressed as a visual angle) in patients' visible pointing deviation between Pre-exposure and Exposure conditions in each session of the first and second week of treatment. A 2×3 ANOVA was performed with the following main effects: week of treatment (first and second) and target position (left, centre and right). The results showed a deviation in the same direction as prism-induced error, which indicates a lack of adaptation to prism exposure. This deviation was slightly reduced in the second week, as revealed by the significance of the main effect of week of treatment [$F(1,9) = 6.5$; $P < 0.03$]; rightward deviation was greater in the first (1.3°) than in the second (1°) week of treatment. Moreover, target position was significant [$F(2,18) = 29.3$; $P < 0.000002$]. *Post hoc* comparison showed a more evident lack of adaptation to the right (1.3°) compared with the centre (1°) and the left (1°)

target stimuli ($P < 0.0002$ for both comparisons). The interaction of week of treatment with target position was not significant.

One possible explanation of the lack of an adaptation effect in R.D. is that the effect needed more time to manifest itself in this patient. To verify this hypothesis, the same statistical analysis was conducted on the first three and the last three trials of the Exposure condition. ANOVA was carried out with the following main effects: week of treatment (first and second), Target position (left, centre and right) and trials (first and last). The main effect of trials was significant [$F(1,9) = 404.8$; $P < 0.000001$]: the adaptation effect was more evident in the last (2°) than in the first (5°) trial. Moreover, the interaction of trials with week of treatment was significant [$F(1,9) = 26.5$; $P < 0.0006$]. The difference between the first three and the last three trials was greater in the second (6° versus 1.2° , $P < 0.0002$) than in the first (4° versus 3° , $P < 0.04$) week of treatment.

After-effect

The dependent measure in this analysis was the difference (expressed as a visual angle) in the invisible pointing deviation between the Pre-exposure and Post-exposure conditions in each session of the first and second weeks of treatment. A 2×3 ANOVA was performed with the following main effects: week of treatment (first and second) and target position (left, centre and right). Week was not significant: the patient's pointing deviation was similar in the first (-1.7°) and second (-1°) weeks of treatment. Nevertheless, the difference between the Post-exposure and Pre-exposure conditions, in the second as well as the first week of treatment, showed a leftward deviation, i.e. there was an after-effect. Target position was not significant: the after-effect did not differ with respect to the right (-1.3°), central (-1.5°) and left (-1.5°) target stimuli. The interaction of week of treatment with target position was significant [$F(2,18) = 8.34$; $P < 0.003$]. *Post hoc* comparisons showed a stronger after-effect in the first week than in the second week of treatment for the right (-1.9° versus -0.7° , $P < 0.0002$) and central (-1.8° versus -1.2° , $P < 0.03$) target stimuli. No significant difference was found between the first and second weeks of treatment for the left (-1.6° versus -1.3°) target stimuli.

To verify a possible difference in the degree of the after-effect in the first three and last three trials, an ANOVA was carried out with the following main effects: week of treatment (first and second), target position (left, centre and right) and trials (first and last). The main effect of trials was significant [$F(1,9) = 51.6$; $P < 0.00005$]. The after-effect was present in the first three trials (-2.5°) but was drastically reduced in the last three trials (-1°). This pattern of results was found for both the first and the second week of treatment.

Duration of the after-effect

To determine the duration of the post-adaptation after-effect, an ANOVA was performed on the patient's displacement expressed as a visual angle with interval as the main effect. The patients' displacement (invisible pointing) was measured before the beginning of treatment (baseline condition), immediately after treatment and 6, 12 and 84 h after treatment. Six hours is the interval between the morning and afternoon sessions of the same day; 12 h is the interval between an afternoon session and the morning session of the following day; and 84 h is the interval between the last afternoon session of the first week and the first morning session of the second week. Interval was significant [$F(4,36) = 30.11$; $P < 0.00(0001)$]. *Post hoc* comparisons showed a leftward deviation of pointing immediately after treatment (-2.3° , $P < 0.0002$) and 6 h (-2.5° , $P < 0.0001$), 12 h (-1° , $P < 0.0003$) and 84 h (-0.5° , $P < 0.02$) after treatment compared with the baseline condition (0.3°). The leftward deviation immediately after treatment (-2.3°) was significantly larger than that found 12 h (-1° , $P < 0.0004$) and 84 h (-0.5° , $P < 0.0001$) after treatment. Similarly, the after-effect 6 h after treatment (-2.5°) was greater than that found 12 h (-1° , $P < 0.0003$) and 84 h (-0.5° , $P < 0.0002$) after treatment. No difference was found in leftward deviation immediately after versus 6 h after treatment.

Discussion

The first aim of the present study was to find out whether the short-term amelioration found after prismatic adaptation in previous studies (Rossetti *et al.*, 1998) can be converted into long-term therapeutic improvement. With this aim, seven patients with a right hemisphere lesion and left visuospatial neglect received treatment with prismatic lenses in twice-daily sessions over a period of 2 weeks. The results showed that 20 training sessions induced long-term improvement in neglect that was fully maintained for at least 5 weeks after treatment. Moreover, some preliminary data (for Patients C.B., R.E., C.T. and F.G.; not reported in this paper) confirm that the amelioration of neglect lasted 17 weeks after the end of treatment. This is the first time that PA has been used as a daily treatment and that its long-lasting effects have been studied.

The improvement found after PA was highly consistent across a wide variety of visuospatial tasks; indeed, it was apparent in each of the tests considered, which assessed different visuospatial abilities, such as those required to bisect a line or to perform simple and complex cancellation and naming tasks. Furthermore, the amount of amelioration found after PA was similar across all tests included in the BIT series (Wilson *et al.*, 1987), with no difference between conventional tests, which are simple pencil-and-paper measures of neglect, and behavioural tests, which reflect aspects of daily life activities. Amelioration of the patients' performance was also observed in other 'ecological' situations, such as the

room description and objects reaching tests. No improvement was found in motor functions (Motricity Index; Demeurisse *et al.*, 1980). However, this aspect needs to be investigated further by increasing the number of patients (only two patients in the experimental group were assessed with the Motricity Index) or by having a more sensitive measure of motor impairment.

A significant improvement after PA training was found in far space (room description test) and in near space (objects reaching test). The amelioration of neglect in personal space (fluff test) was less evident. However, it is worth noting that only four of the six experimental patients showed mild personal neglect, and their neglect improved after PA treatment.

Also, the improvement found after PA was highly consistent across sessions, i.e. immediately after treatment and 2 days, 1 week and 5 weeks after treatment, with a trend to better recovery in the last two sessions. This seems to indicate that the widespread effects of PA on hemispatial neglect remain active after treatment and can be seen as triggering or improving active processes involved in brain plasticity related to multisensory integration and space representation.

At variance with the experimental group, the control group did not show amelioration of neglect symptoms. The control patients, who had stable neglect and received non-specific rehabilitation treatment (general cognitive stimulation and standard physiotherapeutic rehabilitation), performed the tests four times, the same as the experimental patients. Thus, the lack of improvement of neglect in control patients excludes the possibility that the amelioration found in the experimental group can be attributed to the simple presence of general stimulation or to any possible role played by practice effects or learned test responses.

The improvement found after PA in a wide variety of visuospatial tasks confirms and extends previous findings (Rossetti *et al.*, 1998), indicating that the process of PA is not only involved in the recalibration of visuomotor coordination (pointing task) but is also able to affect the organization of higher levels of spatial representation, such as those impaired in neglect patients. In this respect, the present findings, in accordance with recent results of Farnè *et al.* (2002), show that the effects of the PA procedure extend to tests that require visuomotor coordination (cancellation tests and objects reaching test) as well as to tests that do not require a motor response (reading tests and room description test). In other words, the improvement found in the present study was not due to a low-order factor, such as a leftward visuomotor bias—the so-called after-effect. After PA, subjects systematically deviate in the direction opposite to the prismatic shift when manually pointing or reaching for visual objects with the adapted hand. When the adaptation is to a right prismatic deviation, the after-effect consists of a leftward visuomotor bias exhibited by the exposed hand. However, the mechanism of the arm visuomotor bias is an unlikely explanation because this hypothesis predicts an amelioration of neglect symptoms only, or mainly, in those tests involving the use of the adapted

hand (i.e. cancellation, writing and drawing tests). In contrast, in the present study, an improvement was also found in tests that did not require a hand motor response, such as the visuoverbal tasks (i.e. word and non-word reading, menu reading, article reading and the room description test). Therefore, we maintain that the cognitive effects induced by the PA technique can directly influence a relatively high-order level of visuospatial representation.

This conclusion is strengthened when the relationship between the amelioration of visual neglect after treatment and the presence of the adaptation effect and the after-effect are considered. Indeed, all patients who showed adaptation and the after-effect manifested a reduction of neglect after treatment. However, it is worth noting that neglect amelioration was fully maintained for 5 weeks after treatment, whereas the after-effect lasted only 12 h (-1.3°). When the after-effect was tested 84 h after treatment (-1°) it was not significantly different from that found in the baseline condition (0°). Moreover, when the after-effect found immediately after the treatment (-2.7°) was compared with that found 6 h (-1.4°) and 12 h (-1.3°) after treatment, it became evident that the after-effect decayed with time. This implies that the after-effect follows the classical memory decay curve (Kornheiser, 1976). The rate at which the decay takes place seems to be highly variable. Indeed, some patients (C.T. and F.G.) showed a reduction in the after-effect 6 h after treatment, whereas others (R.E. and C.A.) showed a leftward after-effect 168 h after treatment.

At variance with the after-effect, which decayed with time, neglect symptoms seemed to ameliorate with time. In many visuospatial tests, the patients' performance was more accurate 1 or 5 weeks after treatment than immediately after it. This means that, once the mechanism responsible for the recovery of neglect has been implemented, it continues to exert its effect after the treatment procedure has been completed.

The lack of correlation between the duration of neglect amelioration and the duration of the visuomotor after-effect found in the present study can be explained by the effects of PA on two independent levels of cognitive function: low-order functions, i.e. sensory motor coordination, and high-order functions, i.e. spatial representation. In the present study, the effects of PA on low-order functions were short-lasting, whereas its effects on high-order functions were long-lasting.

One of the mechanisms proposed (Rossetti *et al.*, 1998) to account for the improvement in neglect after PA is that PA acts as a lateralized warning signal. The visual–proprioceptive discrepancy induced by prism exposure between the expected position of the hand and its shifted position indicates to the patient that their actual action is biased towards the right compared with their intention. The brain has a natural tendency to compensate for distortions occurring on either the sensory side (vision and proprioception) (Redding *et al.*, 1996) or the motor side (Coello *et al.*, 1996). Consequently, the lateralized sensory–motor information induced by prism

exposure in the pointing task may introduce a signal that is useful for the brain in order to stimulate the correction of left neglect (bottom-up mechanism).

Another hypothesis is that the improvement in neglect after PA is linked to the ocular system. Neglect patients frequently show both gaze and postural bias towards the right side. Manoeuvres such as caloric vestibular stimulation (Cappa *et al.*, 1987; Vallar *et al.*, 1990) and the induction of optokinetic nystagmus (Pizzamiglio *et al.*, 1990), which produce eye deviation towards the neglected side, also produce a temporary reduction in neglect. Moreover, Meador *et al.* (1987) found that, in a representative task in which the patient was asked to imagine the street leading to his house and to name the buildings on the street, recall of items lying in the left hemispace improved when the patient rotated his eyes to the left. Thus, the direction of eye movement can influence spatial representation. This hypothesis can also explain why the patients' performance was more accurate after 1 or 5 weeks than immediately after treatment. Indeed, if PA induces facilitation of ocular movements towards the neglected half-space, the ocular system receives more information from the impaired half-space after PA treatment than before it. As a consequence, the ocular system, stimulated by items arranged in the left hemispace, is induced to re-explore, more accurately, that side of space. Although the patients' eye movements before and after PA were not studied in the present experiment, the possibility that prismatic lenses induce eye deviation needs to be addressed in the near future.

Although PA treatment was effective in most experimental patients, one patient (R.D.) failed to show improvement. This failure can be understood by considering the relationships among the adaptation effect, the after-effect and neglect amelioration. Indeed, the adaptation effect in this patient was partial because the pointing responses in the Exposure conditions always deviated to the right, although the deviation was less pronounced when the last three trials were considered. The after-effect was very unstable and it disappeared after the first few trials. This pattern of results is at variance with that documented in patients who show recovery of neglect after PA treatment. These patients were fully adapted to the prismatic deviation and the after-effect was very stable, with no difference between the first and last trials.

Another possible reason for R.D.'s failure to improve after PA treatment is the nature of his lesion. R.D. had a cerebral lesion, involving the frontotemporal and parietal lobes, that was bigger than those of the experimental patients who showed neglect improvement. Nevertheless it is difficult to say which factor was responsible for the lack of improvement in R.D. In order to understand the functional relationship between PA and the amelioration of visuospatial deficits, it is important to study more extensively patients who do not respond positively to PA.

In conclusion, the present results show that 2 weeks of training with prismatic lenses induced long-term improvement in neglect. Moreover, PA also produced a generalized

beneficial effect both in conventional and in behavioural tests in near as well as in far space, and it is therefore a good candidate treatment for the rehabilitation of patients with neglect. The first advantage of PA, which can be considered a bottom-up treatment, is that the effects following PA can be obtained with a short period of training (2 weeks). Treatments based on top-down mechanisms also led to a stable improvement in neglect that extended to untrained tasks and to functional situations, but in these studies the patients became aware of their difficulties and started to develop voluntary strategies to overcome the deficit after a considerably longer period of training, of 5–8 weeks (Pizzamiglio *et al.*, 1989, 1992; Antonucci *et al.*, 1995).

The second advantage of PA is that it does not require the voluntary orientation of attention to the affected side, which can be difficult for neglect patients. For this reason, treatments based on bottom-up mechanisms, such as PA (and vestibular and optokinetic stimulation, left-sided transcutaneous mechanical vibration, left-sided electrical nervous stimulation and left-limb proprioceptive stimulation), might be more successful because they require less attentional resources. The advantage of bottom-up-based treatments over top-down treatments has been documented (Antonucci *et al.*, 1992). Antonucci and colleagues submitted a group of neglect patients to repeated optokinetic stimulation for 8 weeks and they found a greater improvement in visual neglect compared with a standard treatment. However, optokinetic stimulation is a method that is not easy to use. Therefore, the third advantage of PA, compared with other bottom-up rehabilitative procedures, e.g. optokinetic and vestibular stimulation, is that it is non-invasive and can be performed at home by the patient with no need for hospitalization and without the aid of a therapist.

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